Listing of Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

1-32. (Canceled)

33. (Previously amended) A method of preparing a bi-specific Fab-scFv fusion protein having at least one arm that specifically binds a targeted tissue and at least one other arm that specifically binds a targetable conjugate which comprises a carrier portion which comprises or bears at least one epitope recognizable by said at least one other arm of said bi-specific antibody or antibody fragment, and one or more conjugated therapeutic or diagnostic agents, or enzymes, comprising:

(1) (A) introducing into a mammalian host cell a recombinant DNA construct comprising an expression cassette capable of producing in said host cell a fragment of said bi-specific fusion protein, wherein said construct comprises, in the 5' to 3' direction of transcription, a transcriptional initiation regulatory region functional in said mammalian host cell, a translational initiation regulatory region functional in said mammalian host cell, a DNA sequence encoding a scFv linked to a Fd fragment, and a transcriptional and translational termination regulatory region functional in said mammalian host cell, wherein expression of said fragment of said bi-specific fusion protein is under the control of said regulatory regions;

(B) co-introducing into said mammalian host cell a recombinant DNA construct comprising an expression cassette capable of producing in said mammalian host cell a light-chain antibody fragment which is complementary to said Ed fragment in (A) and which when associated with said Ed fragment forms a Fab fragment whose binding site is specific for said targeted tissue, wherein said construct comprises, in the 5' to 3' direction of transcription, a transcriptional initiation regulatory region functional in said mammalian host cell, a translational initiation regulatory region functional in said mammalian host cell, a DNA sequence encoding a light-chain antibody fragment, and a transcriptional and translational termination regulatory region functional in said mammalian host cell, wherein expression of said light-chain antibody fragment is under the control of said regulatory regions;

(C) growing said cell; and

(D) isolating said bi-specific Fab-scFv fusion protein, or

(2) (A) introducing into a first mammalian host cell a recombinant DNA construct comprising an expression cassette capable of producing in said first mammalian host cell a fragment of said bi-specific fusion protein, wherein said construct comprises, in the 5' to 3' direction of transcription, a transcriptional initiation regulatory region functional in said first mammalian host cell, a translational initiation regulatory region functional in said first mammalian host cell, a DNA sequence encoding a scPv linked to a Fd fragment, and a transcriptional and translational termination regulatory region functional in said first mammalian host cell, wherein expression of said fragment of said bi-specific fusion protein is under the control of said regulatory regions;

(B) introducing into a second mammalian host cell a recombinant DNA construct comprising an expression cassette capable of producing in said second mammalian host cell a light-chain antibody fragment which is complementary to said Ed fragment in (2)(A) and which when associated with said Fd fragment forms a Fab fragment whose binding site is specific for said targeted tissue, wherein said construct comprises, in the 5' to 3' direction of transcription, a transcriptional initiation regulatory region functional in said second mammalian host cell, a translational initiation regulatory region functional in said second host cell, a DNA sequence encoding a light-chain antibody fragment, and a transcriptional and translational termination regulatory region functional in said second mammalian host cell, wherein expression of said light-chain antibody fragment is under the control of said regulatory regions;

(C) growing said first and second mammalian host cells;

(D) optionally isolating said bi-specific fusion protein fragment and said light-chain antibody fragment;

(E) combining said fragments to produce a Fab-scFv bi-specific fusion protein; and

(F) isolating said bi-specific fusion protein.

34. (Previously amended) A method of preparing a bi-specific Fab-scFv fusion protein having at least one arm that specifically binds a targeted tissue and at least one other arm that

specifically binds a targetable conjugate which comprises a cater portion which comprises or bears at least one epitope recognizable by said at least one other arm of said bi-specific antibody or antibody fragment, and one or more conjugated therapeutic or diagnostic agents, or enzymes, comprising:

(1) (A) introducing into a mammalian host cell a recombinant DNA construct comprising an expression cassette capable of producing in said mammalian host cell a fragment of said bi-specific fusion protein, wherein said construct comprises, in the 5' to 3' direction of transcription, a transcriptional initiation regulatory region functional in said mammalian host cell, a translational initiation regulatory region functional in said mammalian host cell, a DNA sequence encoding a scFv linked to a light-chain antibody fragment, and a transcriptional and translational termination regulatory region functional in said mammalian host cell, wherein expression of said fragment of said bi-specific fusion protein is under the control of said regulatory regions;

(B) co-introducing into said mammalian host cell a recombinant DNA construct comprising an expression cassette capable of producing in said mammalian host cell a Fd fragment which is complementary to said light-chain antibody fragment in (A) and which when associated with said light-chain antibody fragment forms a Fab fragment whose binding site is specific for said targeted tissue, wherein said construct comprises, in the 5' to 3' direction of transcription, a transcriptional initiation regulatory region functional in said mammalian host cell, a translational initiation regulatory region functional in said host cell, a DNA sequence encoding a Fd fragment, and a transcriptional and translational termination regulatory region functional in said mammalian host cell, wherein said expression of Fd fragment is under the control of said regulatory regions;

(C) growing said cell; and

(D) isolating said bi-specific Fab-scFv fusion protein, or

(2) (A) introducing into a first mammalian host cell a recombinant DNA construct comprising an expression cassette capable of producing in said first mammalian host cell a fragment of said bi-specific fusion protein, wherein said construct comprises, in the 5' to 3' direction of transcription, a transcriptional initiation regulatory region functional in said first mammalian host cell, a translational initiation regulatory region functional in said first

mammalian host cell, a DNA sequence encoding a scFv linked to a light-chain antibody fragment, and a transcriptional and translational termination regulatory region functional in said first mammalian host cell, wherein expression of said fragment of said bi-specific fusion protein is under the control of said regulatory regions;

(B) introducing into a second mammalian host cell a recombinant DNA construct comprising an expression cassette capable of producing in said second mammalian host cell a Fd fragment which is complementary to said light-chain antibody fragment in (2)(A) and which when associated with said light-chain antibody fragment forms a Fab fragment whose binding site is specific for said targeted tissue, wherein said construct comprises, in the 5' to 3' direction of transcription, a transcriptional initiation regulatory region functional in said second mammalian host cell, a translational initiation regulatory region functional in said second mammalian host cell, a DNA sequence encoding a Fd fragment, and a transcriptional and translational termination regulatory region functional in said second mammalian host cell, wherein expression of said Fd fragment is under the control of said regulatory regions;

(C) growing said first and second mammalian host cells;

(D) optionally isolating said bi-specific fusion protein fragment and said Fd fragment; and

(E) combining said fragments to produce a bi-specific Fab-scFv fusion protein; and

(F) isolating said bi-specific fusion protein.

35-36. (Canceled)

37. (Previously amended) The method of claim 33, wherein said at least one arm that specifically binds a targeted tissue is a humanized Fab fragment.

38. (Canceled)

39. (Previously amended) The method of claim 33, wherein said at least one other arm specifically binds said epitope of said targetable conjugate, and said epitope comprises a peptide.

40. (Previously amended) The method of claim 33, wherein said at least one other arm specifically binds said epitope of said targetable conjugate, and said epitope comprises a carbohydrate.

41. (Previously amended) The method of claim 33, wherein said at least one other arm specifically binds said epitope of said targetable conjugate, and said epitope comprises a hapten.

42. (Previously amended) The method of claim 33, wherein said at least one other arm specifically binds said epitope of said targetable conjugate, and said epitope comprises a chelator or a metal-chelate complex.

43. (Previously amended) The method of claim 42, wherein said chelator is a hard base chelator for a hard acid cation.

44. (Previously amended) The method of claim 42, wherein said chelator is a soft base chelator for a soft acid cation.

45. (Previously amended) The method of claim 43, wherein said chelator is a hard base chelator that comprises carboxylate and amine groups.

46. (Previously amended) The method of claim 43, wherein said hard base chelator is DTPA, NOTA, DOTA or TETA.

47. (Previously amended) The method of claim 33, wherein said at least one other arm specifically binds a tyrosyl-lysine dipeptide.

48. (Previously amended) The method of claim 33, wherein said at least one other arm specifically binds Tyr-Lys(DTPA)-N11$_2$, or Lys(DTPA)-Tyr-Lys(DTPA)-NH_2.

Conclusion

In view of the above remarks and amendments, it is respectfully submitted that this application is in condition for allowance. Early notice to that effect is earnestly solicited. The Examiner is invited to telephone the undersigned at the number listed below if the Examiner believes such would be helpful in advancing the application to issue.

Please direct all correspondence to the undersigned attorney or agent at the address indicated below.

Respectfully submitted,

Date: September 21, 2005

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